Case Report

Sensorineural hearing loss in a child with congenital hypothyroidism receiving thyroid hormone replacement therapy

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ABSTRACT

Background: Congenital hypothyroidism remains as one of the most common causes of hearing loss in children, considering that thyroid hormone plays an essential role in the development and maturation of auditory organs. **Purpose:** To report a case of hearing loss in a child with congenital hypothyroidism who had received thyroid hormone replacement therapy. **Case report:** Presenting a 3-year-old boy with congenital hypothyroidism, growth and developmental delays, and a very severe bilateral sensorineural hearing loss. He was diagnosed at 6 months old, and even after subsequent therapies, the hearing impairment of the child remained profound. **Clinical question:** Could thyroid hormone replacement therapy improve the prognosis of hearing function in congenital hypothyroid patients accompanied by sensorineural hearing loss? **Review method:** Literature review through database PubMed, ProQuest, EBSCO, EBSCOhost and Embase, using keywords: "congenital hypothyroidism", "hearing loss", and "thyroid hormone replacement therapy". **Result:** Screening on 1088 articles found no studies that were relevant with the clinical question and inclusion criteria. **Conclusion:** This report supported the evidence on the effects of congenital hypothyroidism on hearing loss, and the importance of early diagnosis and prompt treatment in congenital hypothyroid children. A missed diagnosis of congenital hypothyroidism in neonates may result in unfavorable effects on the child's growth and development. Further studies are needed to assess the improvement of hearing function in congenital hypothyroid patients accompanied by sensorineural hearing loss that received thyroid hormone replacement therapy.

Keywords: congenital hypothyroidism, hearing loss, thyroid hormone replacement therapy

ABSTRAK

Latar belakang: *Hipotiroidisme kongenital merupakan salah satu penyebab paling umum gangguan pendengaran pada anak-anak, terutama mengingat hormon tiroid berperan penting dalam perkembangan dan maturasi organ pendengaran.* ***Tujuan:*** *Melaporkan satu kasus gangguan pendengaran pada anak dengan hipotiroidisme kongenital yang menetap setelah terapi sulih hormon tiroid.* ***Laporan kasus:*** *Seorang anak laki-laki berusia 3 tahun dengan hipotiroidisme kongenital yang mengalami keterlambatan pertumbuhan dan perkembangan, dan gangguan pendengaran tipe sensorineural bilateral derajat sangat berat. Pasien didiagnosis pada usia 6 bulan, dan walaupun setelah terapi, gangguan pendengaran pada anak tersebut menetap.* ***Pertanyaan klinis:*** *Apakah terapi sulih hormon tiroid mempengaruhi prognosis perbaikan fungsi pendengaran pada pasien hipotiroid kongenital yang disertai gangguan pendengaran sensorineural?* ***Tinjauan literatur:*** *Melalui* database PubMed, ProQuest, EBSCO, EBSCOhost *dan* Embase*, menggunakan kata kunci: "hipotiroidisme kongenital", "gangguan pendengaran", "terapi sulih hormon tiroid".* ***Hasil:*** *Setelah skrining 1088 artikel, tidak ada penelitian yang sesuai dengan pertanyaan klinis dan kriteria inklusi.* ***Kesimpulan:*** *Laporan ini menambah bukti tentang efek hipotiroidisme kongenital pada gangguan pendengaran, serta pentingnya diagnosis dini dan pengobatan segera pada anak hipotiroid kongenital. Diagnosis hipotiroidisme kongenital yang tidak terdeteksi pada neonatus, dapat mengakibatkan efek buruk pada*

pertumbuhan dan perkembangan anak. Diperlukan penelitian lebih lanjut untuk menilai prognosis peningkatan fungsi pendengaran pada pasien hipotiroid kongenital dengan gangguan pendengaran sensorineural, yang mendapatkan terapi sulih hormon tiroid.

Kata kunci: *hipotiroid kongenital, gangguan pendengaran, terapi sulih hormon tiroid*

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INTRODUCTION

Thyroid hormone is an essential part of the human physiological system, and its deficiency is known to induce multiple organ dysfunctions, including the auditory system. In the auditory system, thyroid hormone contributes to the morphogenesis, synaptogenesis, development, and the maturation of auditory pathways,[1,2] hence its deficiency has been postulated to be associated with hearing loss due to the low levels of free T4 (FT4) hormone.[3,4]

Congenital hypothyroidism is one of the most common neonatal endocrine disorders, affecting about 1 in 4000-5000 births worldwide.[5] A similar survey in Indonesia revealed that about 1 in 2736 infants were born with this condition.[6] The rate, type, and severity of hearing loss in children with congenital hypothyroidism varies widely, ranging from mild conductive hearing loss to severe sensorineural hearing loss.[7] Cooper et al.[8] reported that as many as 25% of children with congenital hypothyroidism had mild-to-moderate hearing loss. Out of these, 50% had sensorineural hearing loss and the other 50% had conductive hearing loss.[8] On the other hand, Malik et al.[9] revealed that about 55% children with congenital hypothyroidism had subjective bilateral hearing loss, where 30% of which improved after levothyroxine administration.

Hearing loss in children, including those with congenital hypothyroidism, predisposes the children to developmental delays and disorders such as delayed speech, mental and cognitive retardation, as well as social and communication difficulties.[1,10] These complications are more commonly seen in children receiving delayed treatment,[10] thereby emphasizing the importance of prompt treatment with thyroid hormone replacement therapy in children diagnosed with congenital hypothyroidism.

The authors would like to report a case of a very severe sensorineural hearing loss in a child with congenital hypothyroidism who had received thyroid hormone replacement therapy.

CASE REPORT

A 3-year-old boy was taken to the ear, nose, and throat clinic for routine visits. The patient had been referred to Audiology clinic since the age of six months due to speech delay and hearing problems. His parents reported that the boy was not being able to speak at all, and did not respond to any sound since birth. He was born at term (38 weeks) through normal delivery, with 2800 grams birth weight, and was reported to cry immediately after birth. The pregnancy and the perinatal period were uneventful. However, the patient's growth and development from birth to six months of age were delayed. He was not being able to babble until the age of six months, although he was able to give a sign to show that he wanted something.

At six months of age, the patient underwent thyroid function test due to suspicion of congenital hypothyroidism, and the results revealed a low FT4 (0.90 ng/dL) and a low TSH hormones (5.91 U/mL). At the same year, the patient was diagnosed with malnutrition and pulmonary tuberculosis, and received anti-tuberculosis drugs. After a few days of treatment, the patient showed symptoms of adverse drug reactions and his liver enzymes increased by 10-folds. Subsequently, the drugs were stopped for a week, and the treatment was continued with a minimum-dose regimen. Levothyroxine was initiated at the age of eight months, and the TSH and FT4 levels were followed-up monthly.

At one year old, the patient underwent comprehensive hearing examinations. Distortion Product Otoacoustic Emission (DPOAE) examination revealed impaired hair cells outside the cochlea in both ears. Brainstem Evoked Response Auditory (BERA) examination with stimulus click revealed that wave V were not detected up to 90 dB in both ears, indicating a very severe bilateral sensorineural hearing loss. (Figure 1), and Auditory Steady State Response (ASSR) examination revealed that the hearing threshold of both ears was >110 dB (Figure 2). Based on the examinations, the patient was then fitted with hearing aids from the age of 1.5 years old. A repeated ASSR examination was performed 2 years after hearing aid fitting, of which the results indicated that the hearing threshold of both ears remained >110 dB (Figure 3).

The patient underwent several imaging examinations at the age of two years old. Ultrasound examination of the thyroid gland showed hypoplastic thyroid glands, while the mastoid computed tomography (CT) scan and the brain magnetic resonance imaging (MRI) showed normal results. The mastoid CT scan revealed that both ears' cochlear semicircular canals were well-formed, the cochlea making 2.5 turns around its axis and the length of the right and left cochlear duct were 39.03 mm and 36.50 mm, respectively, without any signs of sclerosis or interspersion in the mastoid water cells. Meanwhile, based on the MRI, the size of both the right and left cochlear nerves were 0.13 cm and was bigger than the facial nerves. No pathological lesions were visible on the brain MRI. At this age, the FT4 and TSH levels of the patient remained steady within normal limits. As it was, the patient was only able to raise his head after the age of 18 months.

At the latest visit, the patient was able to raise his head, sit and stand up with support.

The aim of this case report was to present a case of hearing loss in a child with congenital hypothyroidism who had received thyroid hormone replacement therapy.

CLINICAL QUESTION

Could thyroid hormone replacement therapy improve the prognosis of hearing function in congenital hypothyroid patients accompanied by sensorineural hearing loss?"

PICO formulation:

P: Congenital hypothyroid children with sensorineural hearing loss.

I: Thyroid hormon replacement therapy

C: -

O: Improvement of hearing function

METHOD

The literature search was conducted on PubMed, ProQuest, EBSCO, EBSCOHost and Embase. Based on clinical questions: Could thyroid hormone replacement therapy improve the prognosis of hearing function in congenital hypothyroid patients accompanied by sensorineural hearing loss?"

After literature search, 1088 articles were found, and proceeded with screening for duplication and abstract reading. Full text reading carried out on 48 articles, four articles were obtained, but then excluded because not relevant with PICO. There was no appropriate study obtained.

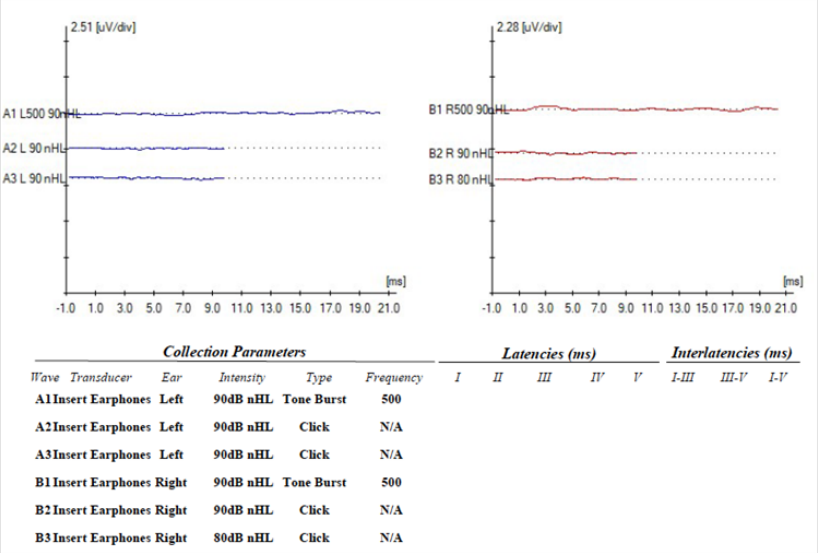

Figure 1. Results of the brainstem evoked response auditory (BERA) click examination showing undetected V waves up to 90 dB in both ears

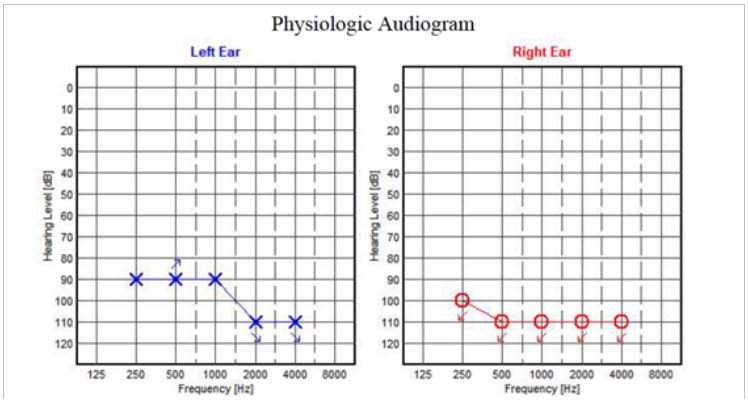

Figure 2. Results of auditory steady state response (ASSR) examination before hearing aid fitting showing that the hearing threshold of both ears was more than 110 dB

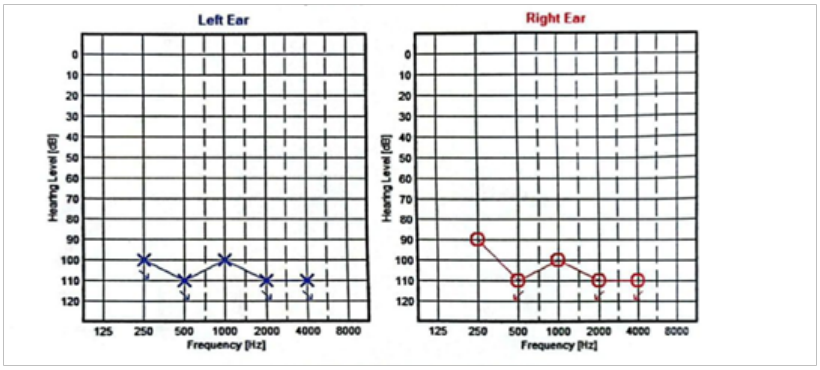

Figure 3. Results of auditory steady state response (ASSR) examination after hearing aid fitting showing that the hearing threshold of both ears was more than 110 dB

DISCUSSION

To this date, the national guideline recommends routine congenital hypothyroidism screening in all neonates to prevent growth and mental retardation. The screening is to be performed between the first 48-72 hours of life through blood collected on a filter paper. A TSH level of ≥20 μU/mL indicates a possibility of congenital hypothyroidism, and the patient should be further evaluated with a repeated TSH assay and a serum FT4 level test.

A low serum FT4 level or a normal serum FT4 level with a high TSH level (≥20 μU/mL) on the confirmatory test supports the diagnosis of congenital hypothyroidism, thus thyroid hormone replacement therapy should be promptly initiated in these patients.[6] In this case report, we described a case of missed diagnosis in which the child was diagnosed with congenital hypothyroidism at the age of six months, where growth and developmental retardation had already manifested.

Thyroid hormone is known to have an important role in the embryology of the ear. Previous studies have shown that thyroid hormone contributes to the development of cochlea, tympanic membrane, immature ossicles, and middle ear mesenchymes.[11,12] In this context, children with congenital hypothyroidism are at a higher risk of developing hearing loss as the development and the maturation of auditory organs are stunted. This is proven by the relatively high frequency of co-existence between congenital hypothyroidism and hearing loss.[13] This is remarkably important considering that hearing loss, especially in childhood, may cause deleterious effects on the child's growth and development including difficulties in receptive language as well as hearing and reading processes.[2,14] This further highlight the importance of timely treatment in children with congenital hypothyroidism, especially considering that the severity of congenital hypothyroidism and the child's age at treatment initiation is directly associated with the degree of hearing loss.[15] In our presented case, the patient first referred to us at the age of 6 months where growth and developmental disorders had occurred. As the patient's auditory organs had been damaged, it became difficult to rehabilitate the patient's hearing ability.

Until now, the extent to which thyroid hormone replacement therapy may improve congenital hypothyroidism patients' hearing ability remains uncertain. Hussein et al.[4] found that about 48% of adults with hypothyroidism had an improvement in their auditory functions following levothyroxine therapy. In addition, the study also found that 15% of the patients' hearing levels returned to baseline after therapy. Similarly, Singh et al.[7] found that thyroid hormone replacement therapy successfully improved the hearing of about 46.4% hypothyroid patients. These improvements were not only seen in patients with sensorineural hearing loss, but also in patients with conductive and mixed hearing loss.[4]

On the other hand, Anand et al.[16] stated that, while hearing recovery following thyroid hormone replacement therapy was possible, such improvements were not seen in some children after subsequent BERA examinations. This was further proven by Chou et al.[17] who found that about 1 in 4 children with congenital hypothyroidism failed to attain hearing improvements following early levothyroxine therapy. In their study, based on BERA examinations, the authors found that the latency period of wave I, III, and V of the congenital hypothyroid patients lengthened. The lengthening of wave I latency might be caused by middle ear inflammation or abnormalities in the inner ear and/or the vestibulocochlear nerve, while the lengthening of wave III and V latency might be induced by aberrations of brainstem maturation. This was similar to our case where the wave V latency of the patient's ears was

prolonged, indicating that there was indeed a damaged central nervous system. According to Chou et al.[17], the administration of thyroid hormone replacement therapy in congenital hypothyroid children within the first three months of life is essential to diminish the adverse effects on brain development. The initiation of levothyroxine therapy after this period may not result in a good hearing prognosis, and the children could suffer from permanent hearing loss.[18]

This might explain our observation where our patient's hearing ability, along with his growth and development, failed to improve even after levothyroxine therapy. In this case, it was presumable that the child's hearing function may remain severely, permanently impaired.

Our case report further added to the evidence of the impact of congenital hypothyroidism on hearing function and the importance of early treatment in children with congenital hypothyroidism. Until recently, evidence on the extent to which thyroid hormone replacement therapy may improve hearing function in children with congenital hypothyroidism remains unclear. Further research is necessary to assess the factors influencing the effects of thyroid hormone replacement therapy on hearing ability in children with congenital hypothyroidism.

REFERENCES

1. Andrade CLO, Alves C de AD, Ramos HE. Congenital Hypothyroidism and the Deleterious Effects on Auditory Function and Language Skills: A Narrative Review. Front Endocrinol (Lausanne). 2021; 12(August): 1-6.
2. de Andrade CLO, Machado GC, Fernandes L da C, de Albuquerque JM, Casais-E-Silva LL, Ramos HE, et al. Mechanisms involved in hearing disorders of thyroid ontogeny: A literature review. Arch Endocrinol Metab. 2017; 61(5): 501-5.
3. Braga H, Duarte JL, da Cruz Fernandes L, Salles IC, Oliveira de Andrade CL, Ramos HE, et al. Congenital hypothyroidism as a risk factor for hearing and parents' knowledge about its impact on hearing. J Otol. 2021; 16(2): 71-9.
4. Hussein MM, Asal SI, Salem TM, Mohammed AM. The effect of L-thyroxine hormone therapy on hearing loss in hypothyroid patients. Egypt J Otolaryngol. 2017; 33(4): 637-44.
5. Hashemipour M, Hovsepian S, Hashemi M, Amini M. Hearing Impairment in Congenitally Hypothyroid Patients. 2012; 22(1): 92-6.
6. Peraturan Menteri Kesehatan Republik Indonesia Nomor 78 Tahun 2014 tentang Skrinning Hipotiroid Kongenital. Jakarta; 2014.
7. singh R, Aftab M, Jain S, kumar D. Audiological Evaluation in Hypothyroid Patients and Effect of Thyroxine Replacement Therapy. Indian J Otolaryngol Head Neck Surg. 2019; 71 (April 2012): 548-52.
8. Cooper HE, Kaden E, Halliday LF, Bamiou DE, Mankad K, Peters C, et al. White matter microstructural abnormalities in children with severe congenital hypothyroidism. NeuroImage Clin. 2019;24 (September 2018): 101980.
9. Malik V, Shukla GK, Bhatia N. Hearing profile in hypothyroidism. Indian J Otolaryngol Head Neck Surg. 2002; 54(4): 285-90.
10. Thakur PK, Nishad RK, Jain AK. Evaluation of Hearing Loss in Congenital Hypothyroid Children at a Tertiary Care Hospital in Central India. Indian J Otolaryngol Head Neck Surg. 2022; 06(January 2022). Available from: https://doi.org/10.1007/s12070-021-03063-0
11. Ru A, Ng L, Goodyear R, Oliver D, Lisoukov I, Richardson G, et al. Retardation of Cochlear Maturation and Impaired Hair Cell Function Caused by Deletion of All Known Thyroid Hormone Receptors. 2001;21 (24): 9792-800.
12. Cordas EA, Ng L, Hernandez A, Kaneshige M, Cheng S, Forrest D. Thyroid Hormone Receptors Control Developmental Maturation of the Middle Ear and the Size of the Ossicular Bones. 2015; 153(March 2012): 1548-60.

13. Lichtenberger-Geslin L, Santos S Dos, Hassani Y, Ecosse E, Abbeele T Van Den, Léger J. Factors associated with hearing impairment in patients with congenital hypothyroidism treated since the neonatal period: A national population-based study. J Clin Endocrinol Metab. 2013;98(9):3644–52.

14. Biswas R, Islam R. Hearing Impairment in Children with Congenital Hypothyroidism. 2020;36(March):14–9.

15. Almagor T, Rath S, Nachtigal D, Sharroni Z, Elias-Assad G, Hess O, et al. High Prevalence of Hearing Impairment in Primary Congenital Hypothyroidism. Eur Thyroid J. 2021;10(3):215–21.

16. Anand VT, Mann SBS, Dash RJ, Mehra YN. Auditory Investigations in Hypothyroidism. 1989;83–7.

17. Chou YH, Wang PJ. Auditory brainstem evoked potentials in early-treated congenital hypothyroidism. J Child Neurol. 2002;17(7):510–4.

18. Bruno R, Aversa T, Catena M, Valenzise M, Lombardo F, De Luca F, et al. Even in the era of congenital hypothyroidism screening mild and subclinical sensorineural hearing loss remains a relatively common complication of severe congenital hypothyroidism. Hear Res. 2015;327(May):43–7.